10/617,546

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NEWS 11	Jun 22	STN Patent Forums to be held July 19-22, 2004

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
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NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
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FILE 'HOME' ENTERED AT 19:43:25 ON 24 JUN 2004

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 19:43:33 ON 24 JUN 2004
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 JUN 2004 HIGHEST RN 698346-19-9
DICTIONARY FILE UPDATES: 23 JUN 2004 HIGHEST RN 698346-19-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> s (salbutamol sulfate)/cn
L1 1 (SALBUTAMOL SULFATE)/CN

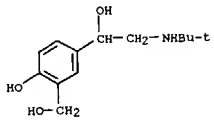
=> d l1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 51022-70-9 REGISTRY
CN 1,3-Benzenedimethanol, α1-[[(1,1-dimethylethyl)amino]methyl]-4-hydroxy-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (±)-Salbutamol sulfate
CN Aerolin
CN Airet
CN Albuterol hemisulfate
CN Albuterol sulfate
CN Almotex
CN Anebron
CN Asmadil
CN Asmalin
CN Asmanil
CN Asmasal
CN Asmatol
CN Asmaven
CN Asmavent
CN Asmidon
CN Asmol Uni-Dose
CN Asthalin
CN Broncho-Spray
CN Broncovaleas
CN Bronter
CN Bugonol
CN Butamol
CN Buto-Asma
CN Butotal
CN Buventol
CN Cetsim
CN Cobutolin
CN Dilatamol
CN dl-Salbutamol sulfate
CN Ecovent
CN Farcolin
CN Grafalin
CN Instavent
CN Libretin
CN Loftan
CN Medolin
CN Mozal
CN Novosalmol
CN NSC 289928
CN Parasma
CN Proventil
CN Respax
CN Salbetol
CN Salbron
CN Salbulin
CN Salbumol
CN Salbusian
CN Salbutalan
CN Salbutamol hemisulfate
CN **Salbutamol sulfate**
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 36519-31-0
MF C13 H21 N O3 . 1/2 H2 O4 S
CI COM

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN (Continued)
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DIOGENES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSPATENTS, IPA, MRCK*, MSDS-OHS, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); USES (Uses)

CM 1

CRN 18559-94-9
CMF C13 H21 N O3



CM 2

CRN 7664-93-9
CMF H2 O4 S

587 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
592 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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=>  fil caplus
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                        ENTRY     SESSION
                                                         7.04        7.25

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 19:45:02 ON 24 JUN 2004
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FILE COVERS 1907 - 24 Jun 2004  VOL 140 ISS 26
FILE LAST UPDATED: 23 Jun 2004  (20040623/ED)
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s 51022-70-9/rn
           592 51022-70-9
             2 51022-70-9D
L2         590 51022-70-9/RN
                 (51022-70-9 (NOTL) 51022-70-9D )

=> s micro?
L3     2056097 MICRO?

=> s l2 and l3
L4         168 L2 AND L3

=> s ?milled
L5       31891 ?MILLED

=> s mill?
L6      245105 MILL?

=> s l3 or l5 or l6
L7     2270835 L3 OR L5 OR L6

=> s l2 and l7
L8         175 L2 AND L7

=> s vapor or gas
         461479 VAPOR
          68434 VAPORS
         502025 VAPOR
                  (VAPOR OR VAPORS)
        1363498 GAS
         470088 GASES
```

```
       1532221 GAS
                 (GAS OR GASES)
L9     1902692 VAPOR OR GAS
 75% OF LIMIT FOR TOTAL ANSWERS REACHED

=> s vapor
        461479 VAPOR
         68434 VAPORS
L10     502025 VAPOR
                 (VAPOR OR VAPORS)

=> s gas
       1363498 GAS
        470088 GASES
SYSTEM LIMITS EXCEEDED - SEARCH ENDED
The search profile you entered was too complex or gave too many
answers.  Simplify or subdivide the query and try again.  If you have
exceeded the answer limit, enter DELETE HISTORY at an arrow prompt
(=>) to remove all previous answers sets and begin at L1.  Use the
SAVE command to store any important profiles or answer sets before
using DELETE HISTORY.

=> s l8 and l10
L11          10 L8 AND L10

=> d l11 1-10 abs ibib
```

L11 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
AB The invention relates to a process for providing a stable crystalline form of a
fine-**milled** salbutamol sulfate, which can be produced, stored and used while maintaining the aerodynamic properties required for inhalation. The process comprises the steps of **micronising** salbutamol sulfate into a particle size required for inhalation, conditioning the salbutamol sulfate by treatment with a water-containing **vapor**, and drying the substance. The relative humidity was kept at ≥55% so that the product recrystd. in 24 h. The stability of the product was dependent on the methods of conditioning.

ACCESSION NUMBER: 2004:60281 CAPLUS
DOCUMENT NUMBER: 140:99665
TITLE: Process for providing a stable crystalline form of salbutamol
INVENTOR(S): Brodka-Pfeiffer, Katharina; Grass, Peter; Haeusler, Heribert; Thieme, Herbert; Langguth, Peter
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006884	A2	20040122	WO 2003-EP6787	20030626
WO 2004006884	A3	20040401		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004052734 A1 20040318 US 2003-617546 20030710
PRIORITY APPLN. INFO.: EP 2002-15701 A 20020712
US 2002-408375P P 20020905

L11 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
AB Interactive mixts. were prepared containing 5% (weight/weight) salbutamol sulfate
using various lactose carrier systems, including sieved fractions and blended mixts. of coarse and fine particles. The solid state and powder properties of the lactose carriers were examined by laser diffraction, differential scanning calorimetry, thermogravimetric anal., powder x-ray diffraction, **vapor** sorption gravimetry, rotating drum and atomic force **microscopy**. The in vitro aerosol deposition was determined using a twin-stage impinger with a Rotahaler at an airflow rate of 60 l/min. The fine particle fraction (FPF) of salbutamol sulfate was determined
using a validated HPLC assay. All samples were highly crystalline with minimal
moisture sorption and the major phase in all samples was α-lactose monohydrate. Significant differences in FPF were observed using the various
carrier systems. FPF increased with decreasing carrier d50% (r2=0.919) and increasing proportion of fine carrier particles (below 5 μm) (r2=0.841). Carriers consisting of very large proportions of fine particles showed low FPF and did not fit the correlation. The presence of
coarse carrier particle fractions was essential to achieve maximum FPF, which
occurred when about 10% of fine carrier particles were present in the mixture Dispersion characteristics may be related to the degree of drug aggregation on the carrier surface.

ACCESSION NUMBER: 2003:60467 CAPLUS
DOCUMENT NUMBER: 139:265576
TITLE: Influence of physico-chemical carrier properties on the in vitro aerosol deposition from interactive mixtures
AUTHOR(S): Louey, Margaret D.; Razia, Sultana; Stewart, Peter J.
CORPORATE SOURCE: Victorian College of Pharmacy, Department of Pharmaceutics, Monash University, Parkville, Vic, Australia
SOURCE: International Journal of Pharmaceutics (2003), 252(1-2), 87-98
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L11 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
AB This study monitored the effect of a series of structurally related surfactants on the crystallization of amorphous salbutamol sulfate. Amorphous
salbutamol sulfate was prepared by spray drying from a solution in water and in
the presence of various alkyl polyglycosides (APGs) at different concns. The particles were then analyzed using isothermal **microcalorimetry** and water **vapor** sorption (Dynamic **Vapor** Sorption, DVS) and near-IR spectroscopy (DVS-NIR). Both isothermal anal. combined with near-IR spectroscopy (DVS-NIR) and DVS-NIR were able to detect the transition from the amorphous to the crystalline state. The presence of APG surfactants
modified the shape of the crystallization peak obtained using isothermal **microcalorimetry**. The gravimetric study combined with NIR revealed that while the crystallization was similar for the particles with or
without surfactant, there was a great difference in the release of water from the newly formed crystal. In the presence of some of the surfactants
tested, salbutamol sulfate released the water much faster than in the absence of surfactant. These results helped to explain the differences found in the isothermal **microcalorimetar** data. Differences were observed in the shapes of the NIR water peaks related to water due to the presence of the surfactant. In conclusion, the use of DVS combined with NIR has helped to analyze and understand the effect of APGs on the crystallization
of amorphous salbutamol sulfate.

ACCESSION NUMBER: 2002:940635 CAPLUS
DOCUMENT NUMBER: 139:154674
TITLE: The effect of alkyl polyglycoside surfactants on the crystallization of spray-dried salbutamol sulphate: a gravimetric near-infrared spectroscopy study
AUTHOR(S): Columbano, Angela; Buckton, Graham; Wikeley, Philip
CORPORATE SOURCE: Dep. Pharmaceutics, Sch. Pharmacy, Univ. London, London, WC1N 1AX, UK
SOURCE: PharmSci [online computer file) (2002), 4(3), No pp. given
CODEN: PHARFY; ISSN: 1522-1059
URL: http://www.aapspharmsci.org/scientificjournals/ph armsci/journal/pdf/ps040316.pdf
PUBLISHER: American Association of Pharmaceutical Scientists
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L11 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
AB The crystallization of amorphous salbutamol sulfate prepared by spray drying was
monitored using a humidity controlled **microbalance** (Dynamic **Vapor** Sorption apparatus, Surface Measurement Systems) combined with a near-IR probe. Amorphous salbutamol sulfate was prepared by spray drying from a solution in water. The particles were then analyzed by SEM, thermogravimetric anal., DSC, powder x-ray diffraction, isothermal **microcalorimetry** and water **vapor** sorption anal. combined with near-IR spectroscopy (NIR). Isothermal **microcalorimetry** and water **vapor** sorption combined with NIR spectroscopy were able to detect the transition from the amorphous to crystalline state. However, while the isothermal **microcalorimeter** showed only a classic crystallization exotherm when the material was exposed at 75% RH, the
DVS-NIR results at the same humidity highlighted a more complex process. When exposed at 75% RH, the uptake of water was followed by crystallization that
was detected using NIR. The expulsion of water after crystallization was very
slow and at a constant rate whether the material was exposed to 75 or 0% RH.
The NIR and DVS studies indicated that the material had crystallized very soon
after exposure to high RH. The water that was expelled during crystallization was
not displaced from the particles and remained associated with the particles
for many days. The use of gravimetric anal. together with NIR spectroscopy provided valuable information on the dynamics of the crystallization
of salbutamol sulfate. The retention of water within recently crystallized
salbutamol is potentially important to the behavior of dosage forms containing
the amorphous (or partially amorphous) form of this drug.

ACCESSION NUMBER: 2002:278840 CAPLUS
DOCUMENT NUMBER: 138:78246
TITLE: A study of the crystallization of amorphous salbutamol
sulphate using water **vapor** sorption and near infrared spectroscopy
AUTHOR(S): Columbano, Angela; Buckton, Graham; Wikeley, Philip
CORPORATE SOURCE: School of Pharmacy, Department of Pharmaceutics, University of London, London, WC1N 1AX, UK
SOURCE: International Journal of Pharmaceutics (2002), 237(1-2), 171-178
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L11 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

AB Particles of an amino acid such as leucine may be formed from an amino acid **vapor**, for example by aerosol condensation, or by spray drying. The amino acid particles have a bulk d. of not more than 0.1 gcm-3 or have a mass median aerodynamic diameter of not more than 10 <mm or are in the form of flakes having a thickness of not more than 100 <mm. The inclusion of the particles of amino acid in powder for use in dry powder inhalers has been found to improve the respirable fraction of the active material in the powder. Ground L-leucine particles were suspended from a fluidized bed by a flow of air and carried in a gas flow into the tube furnace, which was at a temperature ranging from 150-300° and sublimed. The **vapor** emitted from the furnace was mixed with cool air giving a cloud of condensed particles that were subsequently collected in a cyclone and membrane filter. The balk d. of the powder was 0.04 gcm-3. A mixture of salbutamol sulfate and 1% low d. leucine was prepared The powder flow and handling performance of the salbutamol powder was significantly improved, with minimal adhesion to glass walls compared with the **milled** leucine mixture

ACCESSION NUMBER: 2000:401625 CAPLUS
DOCUMENT NUMBER: 133:48937
TITLE: Pharmaceutical powders comprising particles of an amino acid
INVENTOR(S): Ganderton, David; Morton, David Alexander Vodden; Lucas, Paul
PATENT ASSIGNEE(S): Vectura Limited, UK
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000033811	A2	20000615	WO 1999-GB4156	19991209
WO 2000033811	A3	20001012		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9916102	A	20010904	BR 1999-16102	19991209
EP 1137399	A2	20011004	EP 1999-958404	19991209
EP 1137399	B1	20030514		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101591	T2	20011121	TR 2001-200101591	19991209
JP 2002531487	T2	20020924	JP 2000-586305	19991209
AT 240093	E	20030515	AT 1999-958404	19991209
NZ 511965	A	20030926	NZ 1999-511965	19991209
PT 1137399	T	20030930	PT 1999-958404	19991209
ES 2198973	T3	20040201	ES 1999-958404	19991209
AU 770461	B2	20040219	AU 2000-15777	19991209

L11 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

NO 2001002825	A	20010608	NO 2001-2825	20010608
PRIORITY APPLN. INFO.:			GB 1998-27145	A 19981209
			WO 1999-GB4156	W 19991209

L11 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

AB There are described finely divided particles of a pharmaceutical substance, wherein the substance when submitted to water **vapor** gives off heat of less than 1.2 J per g, processes for their production and pharmaceutical formulations containing them. An example is given of salbutamol sulfate (25%) and lactose (75%) conditioned with water at relative humidity 55-65%, nonconditioned **micronized** substance mixture (5-8 J/g) and conditioned **micronized** mixture (<0.5 J/g).

ACCESSION NUMBER: 1999:133202 CAPLUS
DOCUMENT NUMBER: 130:200925
TITLE: Finely divided pharmaceutical particles for inhalation
INVENTOR(S): Briggner, Lars-Erik; Bystrom, Katarina; Jakupovic, Edib; Trofast, Eva; Trofast, Jan
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.
SOURCE: U.S., 7 pp., Cont.-in-part of U.S. Ser. No. 459,660.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5874063	A	19990223	US 1996-606655	19960226
AU 9215347	A1	19921117	AU 1992-15347	19920324
AU 662519	B2	19950907		
EP 580648	A1	19940202	EP 1992-907877	19920324
EP 580648	B1	19960508		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06506454	T2	19940721	JP 1992-507195	19920324
JP 3400999	B2	20030428		
EP 680752	A2	19951108	EP 1995-111178	19920324
EP 680752	A3	19951122		
EP 680752	B1	20011114		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
PL 168232	B1	19960131	PL 1992-301008	19920324
RU 2112507	C1	19980610	RU 1993-58260	19920324
SK 280310	B6	19991108	SK 1993-1088	19920324
CZ 286936	B6	20000816	CZ 1993-2116	19920324
JP 2003155228	A2	20030527	JP 2002-347368	19920324
NO 9303575	A	19931006	NO 1993-3575	19931006
US 5709884	A	19980120	US 1995-379471	19950130
US 5637620	A	19970610	US 1995-459660	19950602
US 5562923	A	19961008	US 1995-479494	19950607
PRIORITY APPLN. INFO.:			SE 1991-1090 A	19910411
			SE 1993-2777 A	19930827
			US 1993-129204 B1	19931025
			US 1995-379471 B3	19950130
			US 1995-459660 A2	19950602
			US 1995-479494 A2	19950607
			SE 1996-141 A	19960116
			CS 1993-2116 A	19920324
			EP 1992-907877 A3	19920324
			JP 1992-507195 A3	19920324
			WO 1992-SE186 A	19920324
			WO 1994-SE780 W	19940825

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS

L11 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

AB Pharmaceutical powders are often **milled** to achieve the optimum particle size. These size reduction processes can introduce dislocations and/or defects onto particle surfaces affecting the overall crystallinity of the powder. If enough energy is imparted, amorphous regions on the particles surfaces may be produced. These amorphous regions have the propensity to absorb significant quantities of water. In this study, the effect of sorbed water on the phys. characteristics of albuterol sulfate was investigated. Phys. properties of this compound were studied in both **micronized** and unmicronized states using SEM, DSC, powder x-ray diffraction, solution **microcalorimetry**, laser diffraction particle size anal. and water **vapor** sorption anal. Subtle differences in crystallinity induced by air jet **micronization** were detected by several anal. methods. Amorphous to crystalline conversions were observed, the kinetic of which are found to be both temperature and relative humidity dependent. These expts. show the dynamic nature of **micronized** albuterol sulfate and acid in the determination of the actual phys. state of this pharmaceutical powder.

ACCESSION NUMBER: 1995:556628 CAPLUS
DOCUMENT NUMBER: 122:298909
TITLE: Process-induced crystallinity changes in albuterol sulfate and its effect on powder physical stability
AUTHOR(S): Ward, Gary H.; Schultz, Robert K.
CORPORATE SOURCE: 3M Pharmaceuticals, St. Paul, MN, 55144-1000, USA
SOURCE: Pharmaceutical Research (1995), 12(5), 773-9
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English

L11 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

AB The present invention relates to a process for providing a stable crystalline form to a fine-grained substance or a substance mixture, which can be produced, stored and used while maintaining the aerodynamic properties required for inhalation of such a substance or a substance mixture, by a) in case of a substance mixture, preparing a homogeneous mixture of the substances; b) **micronizing**, direct precipitating or diminishing by any conventional method the substance or substance mixture into a particle size required for inhalation, the particle size being less than 10 μm; c) optionally preparing a homogeneous mixture of the desired substances when each substance has been introduced from stage b) as sep. fine-grained particles; d) conditioning said substance or substance mixture by treatment with a water containing **vapor** phase in a controlled fashion; and e) drying.

ACCESSION NUMBER: 1995:528673 CAPLUS
DOCUMENT NUMBER: 122:274076
TITLE: Process for conditioning substances
INVENTOR(S): Trofast, Eva Ann-Christin; Briggner, Lars-Erik
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9505805	A1	19950302	WO 1994-SE780	19940825
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9405675	A	19960429	ZA 1994-5675	19940729
TW 427916	B	20010401	TW 1994-83107152	19940804
IL 110698	A1	20021110	IL 1994-110698	19940818
CA 2170394	AA	19950302	CA 1994-2170394	19940825
AU 9476264	A1	19950321	AU 1994-76264	19940825
AU 681186	B2	19970821		
BR 9407320	A	19960416	BR 1994-7320	19940825
EP 717616	A1	19960626	EP 1994-926421	19940825
EP 717616	B1	20010321		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1133004	A	19961009	CN 1994-193793	19940825
CN 1049333	B	20000216		
HU 74000	A2	19961028	HU 1996-447	19940825
HU 217770	B	20000428		
JP 09501930	T2	19970225	JP 1994-507516	19940825
JP 2978247	B2	19991115		
PL 176749	B1	19980730	PL 1994-313142	19940825
RU 2148992	C1	20000520	RU 1996-105935	19940825

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AT 199828	E	20010415	AT 1994-926421		19940825
ES 2156158	T3	20010616	ES 1994-926421		19940825
PT 717616	T	20010830	PT 1994-926421		19940825
CZ 289018	B6	20011017	CZ 1996-544		19940825
SK 283146	B6	20030304	SK 1996-234		19940825
US 5709884	A	19980120	US 1995-379471		19950130
NO 9600744	A	19960223	NO 1996-744		19960223
FI 9600869	A	19960226	FI 1996-869		19960226
CN 1195523	A	19981014	CN 1997-123049		19971126
CN 1090019	B	20020904			
HK 1016493	A1	20030425	HK 1999-101600		19990414
GR 3036106	T3	20010928	GR 2001-400955		20010621
PRIORITY APPLN. INFO.:			SE 1993-2777	A	19930827
			WO 1994-SE780	W	19940825

L11 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

AB Isothermal **microcalorimetry** has been used to monitor the recrystn. of spray-dried salbutamol sulfate. The drug recrystallizes in water **vapor**, by a cooperative process. The cooperative nature demonstrates that the water must first absorb to saturate the entire powder bed before recrystn. occurs. Consequently, recrystn. is slower for low humidities, due to a slower arrival of water **vapor**. The data have been compared with previous data for recrystn. of spray-dried lactose. The heat change for the crystallization was significantly lower for salbutamol sulfate than for lactose. In terms of apparent enthalpy of crystallization, the large exothermic responses are indicative of the fact that the crystal form is the thermodynamically stable state. The salbutamol which had been recrystd. at the lower humidities showed that the process, while being rapid, was discontinuous. In each case, the exothermic recrystn. was followed by an endothermic response for the expulsion of water as the amorphous region recrystd. There was a repeating sequence of crystallization, followed by water expulsion, followed by further recrystn. With each repeat of the cycle the responses decreased in size. This ability to follow crystallization in real time provides a novel insight into the process.

ACCESSION NUMBER: 1995:365096 CAPLUS
DOCUMENT NUMBER: 122:169903
TITLE: The use of isothermal **microcalorimetry** in the study of changes in crystallinity of spray-dried salbutamol sulfate
AUTHOR(S): Buckton, Graham; Darcy, Patricia; Greenleaf, David; Holbrook, Paula
CORPORATE SOURCE: Centre for Materials Science, The School of Pharmacy, University of London, 29-39 Brunswick Square, London, WC1N 1AX, UK
SOURCE: International Journal of Pharmaceutics (1995), 116(1), 113-18
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

L11 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

AB Extending the residence time of drugs delivered to the lungs as inhalation aerosols may results in sustained therapeutic drug levels and reduced toxicity. Droplets were generated from 0.25 wt% disodium fluorescein (DF), and 0.25 wt% albuterol sulfate solns. at a rate of 1 mL min-1 using a Turbotac jet nebulizer. These droplets were dried, concentrated and mixed with saturated lauric acid (LA) **vapor** at both temps. of 60-140°. The resulting coated particles were <5 μm in size as estimated by inertial impaction and SEM. Powder composition, as determined by gas chromatog., ranged from ratios of 1.2:1 to 2.5:1, of LA:DF. Evidence of coating of DF by LA was derived from IR spectroscopy and x-ray **microanal**. Dissoln. studies performed on the coated particles in phosphate buffer, pH 7.4 at 37° and quantified by UV spectroscopy, showed that the half-time for dissoln. (t1/2) increased from 4 min for uncoated DF particles, to 22-55 min for lauric acid coated DF particles, depending on the coating thickness. The t1/2 for albuterol sulfate particles increased from 2.5 min to 12.5 min for albuterol sulfate particles coated with lauric acid at a bath temperature of 100°. Inhalation studies performed on beagle dogs with DF particles coated with lauric acid (bath temperature, 100°) indicated there was a shift and broadening of the peak plasma concentration in comparison with aerosols of DF alone. The average absorption half-time increased from 4.7 min for uncoated DF particles to 11.5 min for lauric acid coated DF particles.

ACCESSION NUMBER:	1994:491637 CAPLUS
DOCUMENT NUMBER:	121:91637
TITLE:	Controlled release from condensation coated respirable aerosol particles
AUTHOR(S):	Pillai, R. S.; Yeates, D. B.; Miller, I. F.; Hickey, A. J.
CORPORATE SOURCE:	Dep. Chem. Eng., Univ. Illinois, Chicago, IL, 60680, USA
SOURCE:	Journal of Aerosol Science (1994), 25(3), 461-77 CODEN: JALSB7; ISSN: 0021-8502
DOCUMENT TYPE:	Journal
LANGUAGE:	English

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	44.76	52.01

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.93	-6.93

STN INTERNATIONAL LOGOFF AT 19:51:20 ON 24 JUN 2004